INCIDENCE AND CLINICAL PREDICTORS OF ATRIAL FIBRILLATION IN PATIENTS WITH DUAL-CHAMBER PACEMAKERS: A RETROSPECTIVE ANALYSIS

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Abstract

Atrial fibrillation (AF) is a prevalent cardiac arrhythmia, affecting millions worldwide and increasing in frequency with age. Despite progress in treatment and prevention, AF remains a significant contributor to stroke, heart failure, and overall cardiovascular morbidity. One particularly challenging type of AF, paroxysmal atrial fibrillation (PAF), is often asymptomatic, leading to delayed diagnosis and increasing the risk of severe complications like stroke. The advent of cardiac implantable electronic devices (CIEDs) has significantly improved the ability to detect subclinical AF or atrial high-rate episodes (AHRE), even in patients with no symptoms. These devices, particularly pacemakers, offer long-term, continuous monitoring of atrial rhythms, making them an invaluable tool for diagnosing AF early and assessing its burden in real time.

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This study focused on a cohort of patients from the Oltenia region who received dual-chamber pacemakers with no prior diagnosis of AF. The research aimed to monitor the incidence of AF in these patients over a follow-up period of 12 to 18 months and to identify potential clinical predictors for developing AF. A total of 91 patients were assessed in this study, all of whom received dual-chamber pacemakers by the pacing guidelines for conditions such as atrioventricular block and sick sinus syndrome. None of the patients had a history of AF at the time of implantation.

Follow-up results indicated an incidence of AHRE in 13.19% of patients, with significant predictors including advanced age and the presence of hypertension. These findings align with the broader literature, which consistently associates both factors with an increased risk of AF. The study underscores the importance of continuous monitoring in pacemaker patients, particularly for detecting asymptomatic AF, which may necessitate specific therapeutic interventions. Although the study's sample size was limited, its findings contribute valuable insights into managing AF in pacemaker patients, particularly regarding early detection and potential risk factors. Future research with larger cohorts is necessary to confirm and expand these results.

Keywords: *dual-chamber pacemaker, atrial fibrillation detection, cardiac implantable electronic devices.*

Rezumat

Fibrilația atrială (FA) este o aritmie cardiacă frecventă, care afectează milioane de persoane în întreaga lume și a cărei incidență crește odată cu vârsta. În ciuda progreselor înregistrate în ceea ce privește tratamentul și prevenția, fibrilația atrială rămâne un factor important pentru accidentul vascular cerebral, insuficiența cardiacă și morbiditatea cardiovasculară generală. Fibrilația atrială paroxistică (PAF), este adesea asimptomatică, ceea ce duce la un diagnostic întârziat și la creșterea riscului de complicații severe, cum ar fi accidentul vascular cerebral. Apariția dispozitivelor electronice cardiace implantabile (CIED) a îmbunătățit în mod semnificativ capacitatea de a detecta FA subclinică chiar și la pacienții care nu prezintă simptome. Aceste dispozitive, în special stimulatoarele cardiace, oferă o monitorizare continuă și pe termen lung a ritmurilor atriale, ceea ce le face un instrument neprețuit pentru diagnosticarea precoce a FA.

Acest studiu s-a axat pe o cohortă de pacienți din regiunea Oltenia care au primit stimulatoare cardiace bicamerale. Cercetarea a urmărit să monitorizeze incidența FA la acești pacienți pe o perioadă de urmărire de 12 până la 18 luni și să identifice potențiali predictori clinici pentru apariția FA. Un total de 91 de pacienți au fost evaluați în acest studiu, toți primind stimulatoare cardiace bicamerale în conformitate cu indicațiile de ghid. Niciunul dintre pacienți nu a avut antecedente de FA la momentul implantării.

Rezultatele urmăririi au indicat o incidență a FA de 13,19% din totalul pacienților, vârsta înaintată și prezența hipertensiunii arteriale fiind caracteristici semnificative statistic la acești pacienți. Aceste constatări se aliniază cu literatura de specialitate, care asociază în mod constant ambii factori cu un risc crescut de FA. Studiul subliniază importanța monitorizării continue la pacienții cu stimulator cardiac, în special pentru detectarea FA asimptomatică, care poate necesita intervenții terapeutice specifice. Deși dimensiunea eșantionului studiului a fost limitată, constatările sale contribuie cu informații valoroase la gestionarea FA la pacienții cu stimulator cardiac, în special în ceea ce privește detectarea precoce a FA și a potențialilor factori de risc. Sunt necesare cercetări viitoare cu cohorte mai mari pentru a confirma și extinde aceste rezultate.

Cuvinte cheie: *stimulator cardiac bicameral, detectarea fibrilației atriale, dispozitive electronice cardiace implantabile.*

Introduction

Despite significant advancements in both treatment and prevention, the global prevalence and impact of atrial fibrillation (AF) continue to increase[1]. AF is a common arrhythmia that affects millions of people worldwide and is characterized by irregular and often rapid heartbeats[2]. The prevalence of AF increases with age, and it is estimated that over 30 million people worldwide have AF[3]. While AF can be asymptomatic, it can lead to various complications, including stroke, heart failure, and other cardiovascular diseases[4]. Paroxysmal atrial fibrillation (PAF) is a type of AF that is typically characterized by brief episodes that last less than seven days and terminate spontaneously. PAF is often asymptomatic, and as a result, it can go undetected for years. However, PAF increases the risk of stroke and heart failure, making early detection and treatment crucial[4].

Cardiac implantable electronic devices (CIEDs) provide long-term, continuous rhythm monitoring with high sensitivity and specificity, making them highly effective for detecting AF and accurately evaluating AF burden[5,6]. Diagnosing AF in pacemaker patients can be challenging, as many episodes of PAF are asymptomatic and may not be detected without appropriate pacemaker programming[7]. Pacemakers can be programmed to detect episodes of AF based on various criteria, including the episode's duration, the ventricular rate during the episode, and the episode's timing relative to other cardiac events[8,9]. In addition, some pacemakers are equipped with algorithms that can distinguish AF from other types of arrhythmias, such as supraventricular tachycardia[10]. When an

episode of AF is detected, the pacemaker can store the data for later review by a physician or can transmit the data wirelessly to a monitoring center for review in real time. The management of AF in pacemaker patients is similar to that of AF in non-pacemaker patients. The goals of management include the prevention of stroke, the reduction of symptoms, and the improvement of overall cardiac function[11].

This study aims to analyze a cohort of patients from the Oltenia region who received dual-chamber pacemakers without a prior diagnosis of AF. Over a follow-up period of approximately 12 to 18 months, the study seeks to monitor the occurrence of AF in these patients and identify potential predictors for this arrhythmia. By focusing on a previously undiagnosed population, the research will contribute to understanding the incidence of AF in pacemaker patients and explore factors that may predispose this group to developing AF over time.

Materials and Methods

Population

We conducted a retrospective observational study at Emergency County Hospital Craiova, Romania. We enrolled 91 adult patients, aged over 18 years, who required cardiac pacing due to third-degree atrioventricular block, second-degree atrioventricular block, sick sinus syndrome, or trifascicular block, by the guidelines for cardiac pacing. Patients were enrolled between October 2020 and October 2022.

Inclusion criteria comprised symptomatic patients with documented indications for permanent cardiac pacing, such as recurrent syncope, presyncope, dizziness, or documented pauses on Holter monitoring. Exclusion criteria included severe infection or patient refusal to participate. Also, patients with a history of paroxysmal atrial fibrillation/atrial flutter, patients with a single-chamber pacemaker, and patients with secondary liver damage were excluded from the study.

All patients provided informed consent for participation in the study, acknowledging the nature of the intervention, potential risks, and benefits. The research adhered to the principles outlined in the Declaration of Helsinki and received approval from the Research Ethics Committee of the University of Medicine and Pharmacy of Craiova regarding opinion number 108/01.03.2024.

Patients enrolled in this study were provided with either the St Jude Endurity MRI dual-chamber pacemaker or Medtronic Sensia/Vitatron. These pacemakers were equipped with advanced diagnostic features specifically designed for automatic AF.

Patient Follow Up

Follow-up assessments were conducted at regular intervals, including visits at one,

	Number	%
Indication for cardiac pacing		
• Atrioventricular Block grade II	24	26.4
• Atrioventricular Block grade III	52	57.1
• Binodal Disease	3	3.3
• Atrial fibrillation with slow ventricular rate	1	1.1
• Sinus Node Disease	10	11.0
• Trifascicular Block	1	1.1
• Total	91	100
Cardiac Pacing		
• DDD	69	75.8
• DDDR	22	24.2
Sex		
• Male	57	62.6
• Female	34	37.4
Age		
• <=70	27	29.7
• >70	64	70.3
Arterial hypertension		
• without	5	5.5
• 1	5	5.5
• 2	27	29.7
• 3	54	59.3
Ejection fraction before cardiac pacing		
• >55%	57	62.6
• 40-55%	34	37.4
• <40%	0	0
Ejection fraction after 3 months		
• >55%	36	39.6
• 40-55%	53	58.2
• <40%	1	1.1
AF/AFL after one month		
• Yes	4	4.4
• No	87	95.6
AF/AFL after three months		
• Yes	10	11.0
• No	80	87.9
AF/AFL after six months		
• Yes	12	13.2
• No	78	85.7
AF>=5 min		
• Yes	9	9.9
• No	82	90.1
AF<5min		
• Yes	12	13.1
• No	80	86.9

Table 1. *The main characteristic of a cohort study*

three, six months, and annually, to evaluate the efficacy and safety of the cardiac pacing intervention. A comprehensive evaluation of clinical outcomes, device function, and any adverse events was performed during each follow-up visit. We assessed patient demographics such as age and gender. We also evaluated the risk of stroke by calculating a CHA2DS2-VAsc score. We assessed the patient's clinical condition using the NYHA functional class. Medical history and an electrocardiogram were obtained at each visit, and a physical examination was also carried out. The attending physicians carefully evaluated the pacemaker's settings to ensure appropriate function, including assessing the presence or absence of improper AF sensing and adjusting pacing and sensing thresholds as necessary.

A series of tests were carried out to obtain precise readings, including assessments for myopotential and ventricular far-field oversensing. These tests were conducted within the standard post-ventricular atrial blanking period of 160 ms. If oversensing was detected in these tests or the pacemaker's data, the atrial blanking and/or atrial sensitivity settings were adjusted accordingly. The pacemaker device was configured to record any instance of atrial tachyarrhythmia that had a sudden onset with a rate surpassing 160 beats per minute (bpm) for at least ten consecutive ventricular beats. An echocardiographic examination was performed before and three months after the cardiac stimulation.

Statistical Analysis

The survey data were processed using SPSS Statistics software (version 29.0. IMB Corp. Armonk, NY, USA). The quantitative variables were checked for normality using the Shapiro–Wilk test. If the normality condition was confirmed, the means were compared using parametric tests: Student's t-test was used for two independent samples, and the Student's *t*-test for Paired Samples was used for two dependent samples. Cross-tabulations were calculated for the qualitative variables. Frequency tables (Crosstab) were produced for the qualitative variables, and the correlation of their attributes was tested with Chi-Square Tests. $p < 0.05$ was considered statistically significant.

Results

Patient characteristics

The study cohort consisted of 91 patients, with a predominant indication for cardiac pacing being Atrioventricular Block grade III (57.1%), followed by Atrioventricular Block grade II (26.4%). Other indications included Binodal Disease (3.3%), Atrial fibrillation with slow ventricular rate (1.1%), Sinus Node

Variable	AHREs (n=12)	No AHREs (n=79)	P-value
Age, years, mean (±SD)	77.67±7.49	72.41±7.98	0.03
Sex n (%)	M=6 (50%), F=6 (50%)	M=51(64.55%),F=28(35.45%)	0.33
NYHA class before cardiac pacing Class I Class II Class III	 2 (16.66%) 7 (58.33%) 3 (25%)	 4 (5.06%) 52 (65.82%) 23 (29.11%)	0.36
NYHA class after one month of cardiac pacing Class I Class II Class III	 1 (8.33%) 11 (91.66%) 0 (0%)	 4 (5.12%) 68 (87.17%) 6 (7.69 %)	0.32
NYHA class prior after three months of cardiac pacing Class I Class II Class III	 2 (16.66%) 8 (66.66%) 2 (16.66%)	 3 (3.84%) 70 (89.74%) 5 (6.41%)	0.82
Cardiac pacing DDD DDDR	 7 (58.33) 5 (41.66)	 62 (78.48%) 17 (21.51%)	0.13
Duration of the QRS complex paced	145.83±8.211	147.29±12.42	0.69
Heart rate mean (±SD)	37.00±8.05	46.04±19.83	0.12
Systolic blood pressure mean, (±SD)	165.42±32.64	140.66±30.64	0.01
Diastolic blood pressure, mean (±SD)	82.50±16.58	79.90±18.03	0.63
Creatinine	1.06±0.29	1.03±0.46	0.81
Mitral regurgitation None Mild Moderate Severe	 2 (16.66%) 6 (50%) 3 (25%) 1 (8.33%)	 5 (6.32%) 52 (65.82%) 19 (24.05%) 3 (3.79%)	0.98
Mitral stenosis None Mild Moderate Severe	 12 (100%) 0 (0%) 0 (0%) 0 (0%)	 75 (94.93%) 3 (3.79%) 1 (1.26%) 0 (0%)	0.45
Aortic regurgitation None Mild Moderate Severe	 11 (91.66%) 1 (8.33%) 0 (0%) 0 (0%)	 66 (83.54%) 7 (8.86%) 5 (6.32%) 1 (1.26%)	0.36

Table 2. *Predictors of atrial high rate events on device interrogation*

Continued table 2

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Aortic Stenosis None Mild Moderate Severe	 11 (91.66%) 1 (8.33%) 0 (0%) 0 (0%)	 74 (93.67%) 0 (0%) 1 (1.26%) 4 (5.06%)	0.64
Tricuspid Regurgitation None Mild Moderate Severe	 4 (33.33%) 5 (41.66%) 2 (16.66%) 1 (8.33%)	 18 (22.78%) 45 (56.96%) 15 (18.98%) 1 (1.26%)	0.95
LVEF, %, mean (±SD) prior to cardiac pacing	54.75±2.30	53.43±4.69	0.31
LVEF, %, mean (±SD) after 3 months of cardiac pacing	51.92±3.5	51.05±4.81	0.55

Table 2. *Predictors of atrial high rate events on device interrogation*

Disease (11.0%), and Trifascicular Block (1.1%). Regarding the pacing modes, DDD pacing accounted for 75.8%, while DDDR pacing was used in 24.2% of cases. Regarding gender distribution, 62.6% were male, and 37.4% were female. The mean age of the study group was 73.10 ±7.08 years. Among patients, 5.5% had no hypertension, 5.5% had hypertension stage 1, 29.7% had hypertension stage 2, and 59.3% had hypertension stage 3. Before cardiac pacing, 62.6% of patients had an ejection fraction greater than 55%, 37.4% had an ejection fraction between 40-55%, and none had an ejection fraction less than 40%. After three months, 39.6% had an ejection fraction greater than 55%, 58.2% had an ejection fraction between 40-55%, and 1.1% had an ejection fraction less than 40%. At one month, 4.4% of patients experienced AF/AFL (Atrial Fibrillation/Atrial Flutter), while 95.6% did not. After three months, 11.0% experienced AF/AFL, and 87.9% did not. Similarly, 13.2% experienced AF/AFL after six months, and 85.7% did not. For AF episodes lasting five minutes or longer, 9.9% experienced such episodes, while 90.1% did not. Conversely, for AF episodes lasting less than five minutes, 12.1% experienced them, while 87.9% did not. The main characteristics

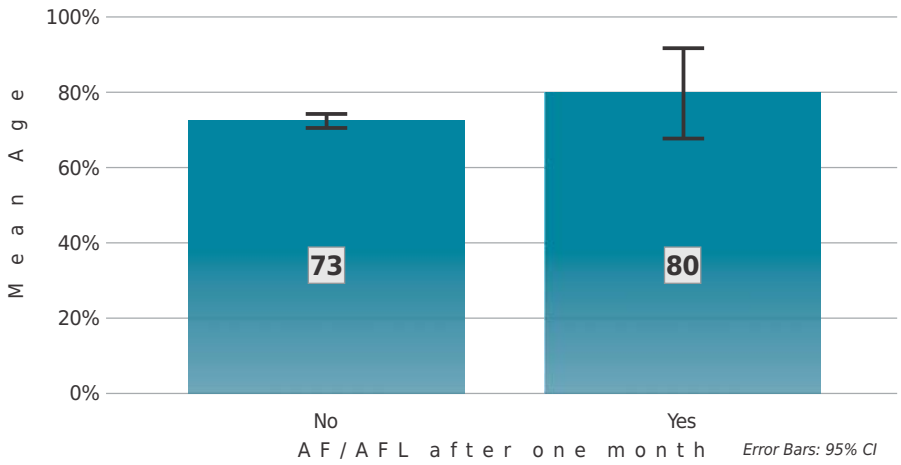

Figure 1. *The mean age of those who developed AF/AFL one month after pacemaker implantation*

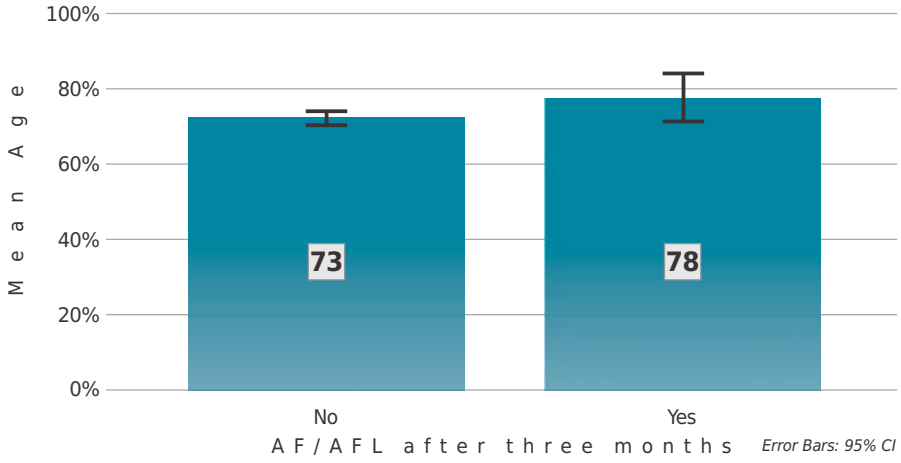

Figure 2. *The mean age of those who developed AF/AFL three months after pacemaker implantation*

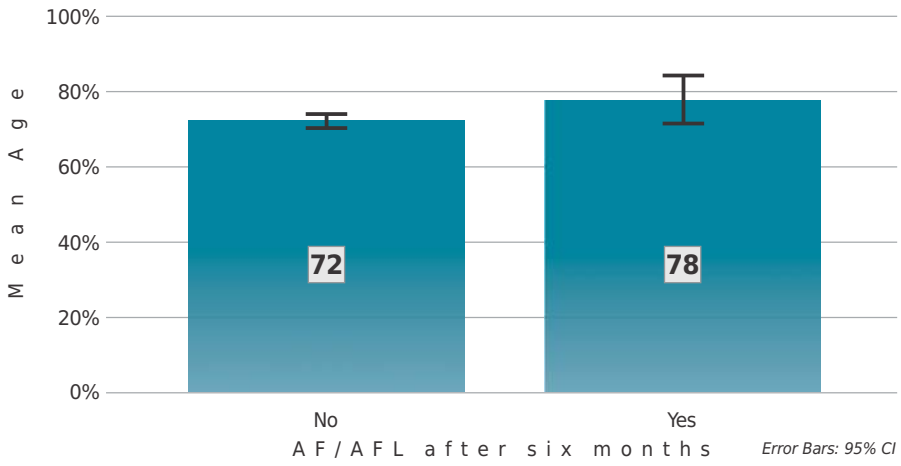

Figure 3. *The mean age of those who developed AF/AFL was six months-one years after pacemaker implantation*

of patients and their preoperative clinical data are presented in Table 1.

Incidence and clinical predictors of AHRE

Out of 91 participants who underwent dual-chamber PPI, 12 (13.19%) patients experienced AHRE lasting <5 minutes from one year after device implantation. Among these patients with AHRE, the majority (9 patients) had episodes lasting more than five minutes. Various demographic, clinical, and echocardiographic parameters were evaluated to identify predictors of AHRE within the population (see Table 2). However, only age (77.67 ± 7.49 vs. 72.41 ± 7.98 years; $p = 0.03$) and systolic blood pressure at presentation (165.42 ± 32.64 vs. 140.66 ± 30.64 mmHg; $p = 0.01$) showed a statistically significant association with AHRE occurrence on independent samples T-test. Other factors such as sex, NYHA class, cardiac pacing mode, duration of the QRS complex, heart rate, diastolic blood pressure, creatinine levels, and valvular parameters did not reach statistical significance.

One month after pacemaker implantation, the average age of those who developed atrial fibrillation was approximately 80. At three months, it was 78, and at six months to one year, it remained 78. In comparison, the average age of those who did not develop atrial fibrillation was 73 at one month, 73 at three months, and 72 at six months to one year. These results can be observed in Figures 1, 2, and 3.

Discussions

AF is the most common cardiac rhythm disorder encountered in clinical practice, accounting for a significant number of physician visits compared to other arrhythmias. It is associated with substantial morbidity and mortality, often leading to complications such as stroke and heart failure[12, 13]. Since the first pacemaker implantation in 1958, pacemaker technology has seen significant advancements, particularly with the introduction of dual-chamber pacemakers, which help maintain atrioventricular synchrony. These devices improve cardiac hemodynamics and reduce the risk of developing AF, heart failure, and stroke compared to single-chamber pacemakers[12, 14]. However, despite advancements in pacemaker technology, including the adoption of dual-chamber pacemakers, these patients have a trend of reduced ejection fraction over time[14]. This decline in cardiac function suggests a potential negative impact of prolonged pacing-induced alterations on cardiac mechanics. Possible contributing factors may include altered ventricular activation patterns, pacing-induced dyssynchrony, and

the detrimental effects of right ventricular pacing on left ventricular function[12], highlighting the need for further investigation into the underlying mechanisms and potential strategies to mitigate these adverse effects.

The decrease in cardiac function can lead to an increase in pressure and volume in the left atrium, which may favor the occurrence of AHRE. Our study noted a difference in ejection fraction between AHRE-positive and AHRE-negative groups, with the former exhibiting a lower ejection fraction; however, this disparity did not reach statistical significance. While this trend suggests a potential association between AHRE and declining cardiac function, further investigation with larger sample sizes may be warranted to elucidate this relationship conclusively. It's also essential to consider that patients requiring pacemaker implantation are typically elderly, with pre-existing conditions such as hypertension and heart disease. These conditions are known risk factors for AF, making this population particularly vulnerable to AF development[15]. Therefore, AF in pacemaker patients is not solely attributable to pacing itself but also to the pre-existing health profile typical of these patients. This understanding underscores the need for a tailored treatment strategy that addresses pacing-related effects and management of coexisting conditions.

Detecting AF episodes in real-world clinical practice can be challenging due to the variation in paroxysmal episodes and the poor correlation between symptoms and true episodes of arrhythmias[10]. While routine 12-lead ECG screening yields limited results, longer monitoring by Holter or intermittent handheld ECG recordings can identify AF more accurately[16]. CIEDs offer longer monitoring time and screening algorithms with intracardiac electrograms to identify atrial high rate (AHR) events[17].

Earlier studies defined device-detected AF as AHR events sustained for a certain duration (usually more than 5 or 6 minutes) to avoid false positives from far-field R wave sensing and noises. However, this approach may exclude real AF events with shorter duration or slower ventricular rates. This study adopted a combined definition of multi-sensing window (MSW) and AHR algorithm, as well as EGM evidence, to collect a more accurate AF burden, demonstrating feasibility and accuracy[15,18].

In the present study, the incidence of AF episodes detected in the patient population was 13.1%, consistent with findings reported in other literature. Previous studies have shown a wide variation in AF prevalence among pacemaker patients, with rates ranging from 10% to 50%[9, 19, 20]. This variability is likely influenced by differences in patient populations, pacemaker settings, and the length of follow-up. Nevertheless, it is evident that AF is common in pacemaker patients and should be carefully considered in their ongoing management[20].

Antiarrhythmic drug therapy, mainly beta-blockers, was administered to some patients as part of their treatment regimen. Antiarrhythmic drugs' specific selection and dosage were determined based on individual patient needs. These medications are aimed at managing and controlling baseline heart conditions as well as symptomatic arrhythmias such as atrial or ventricular extrasystoles or atrial tachycardias within the study population[21].

In our study, atrial fibrillation (AF) was significantly correlated with both age ($p=0.03$) and hypertension ($p=0.01$), findings that are well-supported in existing literature[22-24]. It is widely recognized that the incidence of

AF increases with age, largely due to structural and electrophysiological changes in the atria over time. Hypertension is also a well-established risk factor contributing to atrial remodeling and fibrosis, which predisposes patients to AF.

Limitations of a Single-Center Retrospective Cohort Study

This study has several limitations that should be taken into account when interpreting the results. Firstly, it is a single-center retrospective cohort study, meaning the findings may not be generalizable to other practice settings. Additionally, the sample size and the mean follow-up period are small, which may limit the statistical power of the study and make it difficult to draw definitive conclusions. Another limitation is that the pacemaker default settings for AF detection differed slightly between different models, although devices from only three manufacturers were included. As a result, the findings may not be directly applicable to all real-life decisions and patient management.

Conclusions

Overall, CIEDs offer a valuable tool for detecting AF episodes and assessing AF burden in clinical practice, particularly in patients with subclinical AF and those without a clinical AF history. We found that there is a clear correlation between the incidence of new-onset AF and age and blood hypertension, according to current literature. Despite the study's limitations, it provides valuable insights into the use of pacemakers for AF detection and management, and it is a valuable tool for detecting asymptomatic AF episodes that may need specific therapeutic management. Future studies with larger sample sizes and more diverse patient populations may help to confirm and extend these findings.

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